REMARKS

At page 3, the Advisory Action states:

> Applicants also argue that the references do not teach each and every element of the claimed invention, such as introduction of a nucleic acid encoding an altered human IMPDH into a eukaryotic cell, and the reference of Farazi et al. and Lightfoot do not teach this element. *While this is true*, Roelant et al., the third references in the rejection, discloses this element. Roelant et al. discloses a method of performing proliferation assay by quantifying the number of viable cells which contains heterologous polynucleotides. (*emphasis added*)

In this passage, the Advisory Action consents that introduction of a nucleic acid encoding an altered human IMPDH into a eukaryotic cell is not taught by Farazi et al. or Lightfoot. However, it asserts that this element is taught by Roelant et al. According to the Advisory Action, Roelant et al. teaches a method of quantifying cells "which contains heterologous polynucleotides." After a thorough review, however, Applicant has been unable to find any mention in Roelant et al. of cells that contain heterologous polynucleotides. Further, Roelant et al. clearly does not teach the missing element of an *altered human IMPDH*. Since none of the references cited by the Office Action teach the introduction of an altered human IMPDH into a eukaryotic cell, the combined references do not render the claimed invention obvious.

A telephone interview discussing the above arguments was held on July 13, 2005. During that conversation, Examiner agreed that Roelant et al. do not discuss cells containing heterologous polynucleotides. Based on this discussion, Examiner agreed to withdraw the Advisory Action.

During the telephone interview, Examiner stated that she understands the invention to be a method of screening for new IMPDH mutants. Applicant asserted that

this is an inaccurate description of the invention. In light of this conversation, Applicant wishes to take this opportunity to clarify the invention.

The present application teaches a method for selective proliferation and/or viability of a eukaryotic cell. In this method, a nucleic acid encoding a specific IMPDH mutant is introduced into a first cell, but not a second cell. The specific IMPDH mutant encoded by the nucleic acid is known to be resistant to certain selective conditions. After the nucleic acid is introduced, the first and second cells are exposed to the previously mentioned selective conditions. Following exposure to these conditions, the first cell will exhibit greater proliferation and/or viability than the second cell. The invention does not entail the screening of IMPDH mutants. Rather, it involves the use of specific, known IMPDH mutants to selectively proliferate a cell. Because of this, the present invention differs markedly from the teachings of Farazi et al. and Lightfoot.

Farazi et al. teach inserting random IMPDH mutants into *E. coli* cells and screening the mutants for IMPDH inhibitor resistance. Mutants identified in this manner are used by Farazi et al. "to identify the structural features that determine the species selectivity of MPA" (Farazi, abstract). Farazi et al. do not teach or suggest the insertion of IMPDH mutants identified in this manner into a cell, much less a eukaryotic cell. Farazi et al. merely screen unknown mutants, then characterize their amino acid sequences to determine which residues confer resistance. Farazi et al. certainly does not contemplate the insertion of specific, known IMPDH mutant to selectively proliferate a cell.

Lightfoot teaches the identification of an IMPDH mutant that is resistant to an IMPDH inhibitor by exposing cells to increasing concentrations of IMPDH inhibitors and

isolating IMPDH from those cells that survive. Lightfoot then begins to characterize the molecular changes that give rise to IMPDH inhibitor resistance. Like Farazi et al., Lightfoot merely describes a method of screening for IMPDH mutants with IMPDH inhibitor resistance. Lightfoot does not teach or suggest the insertion of the identified mutant into a cell, much less a eukaryotic cell. Like Farazi et al., Lightfoot certainly does not contemplate the insertion of specific, known IMPDH mutant to selectively proliferate a cell.

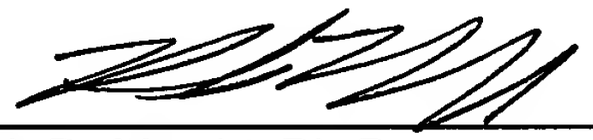
Farazi et al. and Lightfoot identify specific IMPDH mutants and characterize their basic features. However, neither reference teaches or suggests the insertion of known IMPDH mutants into a cell for any purpose, much less to selectively proliferate a cell. In addition, neither reference discusses the insertion of any IMPDH mutant, known or unknown, into a eukaryotic cell.

CONCLUSION

In view of the foregoing, it is submitted that the present claims are in condition for allowance. Accordingly, Applicant respectfully requests that a Notice of Allowance be issued.

Respectfully submitted,
Perkins Coie LLP

Date: July 15, 2005



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